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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/103,745 | 06/24/1998 | SUDHIR AGRAWAL | IDRA-740US1 | 3401 |

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| EXAMINER | |
|---|---|
| WOLLENBERGER, LOUIS V | |
| ART UNIT | PAPER NUMBER |
| 1635 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/103,745 | AGRAWAL, SUDHIR | |
| | Examiner | Art Unit | |
| | Louis V. Wollenberger | 1635 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *10 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3-5 and 16-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1, 3-5, 16-18* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/10/2007 has been entered.

### *Status of Application/Amendment/Claims*

Applicant's response filed 9/10/2007 to the Final Rejection mailed 4/13/2007 is acknowledged. Also acknowledged are Applicant's amendments to the claims.

With entry of the amendment filed on 9/10/2007, Claims 1, 3-5, and 16-18 are now pending and subject to restriction as follows.

### *Election/Restrictions*

> 37 CFR 1.142(a), second sentence, indicates that a restriction requirement "will normally be made before any action upon the merits; however, it may be made at any time before final action. This means the examiner should make a proper requirement as early as possible in the prosecution, in the first action if possible, otherwise, as soon as the need for a proper requirement develops. Before making a restriction requirement after the first action on the merits, the examiner will consider whether there will be a serious burden if restriction is not required. MPEP 811.
>
> Since 37 CFR 1.142(a) provides that restriction is proper at any stage of prosecution up to final action, a second requirement may be made when it becomes proper, even though there was a prior requirement with which applicant

complied. *Ex parte Benke*, 1904 C.D. 63, 108 O.G. 1588 (Comm'r Pat. 1904). MPEP 811.02.

In the instant case, Applicant's amendments to the claims, amending claims 1 and 3-5, and adding new claims 16-18, necessitates the following further restriction requirement. With the entry of the amendments, a serious search and examination burden has become apparent, as explained below.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claim 1, drawn to a modified phosphorothioate oligonucleotide for inhibiting gene expression, wherein the modification is a 2'-O-substituted CpG, classified in class 536, subclass 24.5, for example.

II. Claims 3-5, drawn to a method for providing a modified CpG containing phosphorthioate oligonucleotide to a mammal or to an individual with a disease caused by aberrant gene expression, wherein the modified CpG is an alkylphosphonate CpG, phosphotriester CpG, stereospecific phosphorothioate CpG, phosphoramidate CpG, inverted CpG, or 2'-5'-CpG, classified in class 514, subclass 44, for example. Election of this group requires the further election of a single type of modified CpG, from claims 3, 4, and 5, as explained below.

III. Claims 16-18, drawn to a method for providing a 2'-O-substituted CpG containing phosphorothioate oligonucleotide to a mammal or individual, classified in class 514, subclass 44, for example.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case, each invention is drawn to or comprises the use of 2'-O-substituted CpG containing phosphorothioate oligonucleotides. However, the inventions are, nevertheless, distinct because the product can be used in a materially different process. For example, the product phosphorothioate oligonucleotide can be used as a probe in Northern blotting assays to determine the presence and relative quantity of specific mRNA transcripts, which does not require administering the oligonucleotide to mammals and individuals as in Group III.

Furthermore, searching and examining each of these inventions in a single application presents a serious burden on the examiner, since each group would require different considerations of the patent and non-patent literature with regard to novelty, obviousness, written description, and enablement. Burden as defined in MPEP §803, includes both the search and the examination of each claim with regard to 35 USC §101, 102, 103, and 112. In this respect,the search and consideration of the patentability of claims drawn to products would not necessarily be coextensive nor require the same analysis as that for claims drawn to methods of using those products.

Therefore, because these inventions are distinct for the reasons given above, and the searches required for each are divergent and not coextensive, and because a search and

examination of each of the Inventions in a single application would present a serious burden on the Examiner, restriction for examination purposes as indicated is proper.

Inventions I and II are directed to an unrelated product and process. Product and process inventions are unrelated if it can be shown that the product cannot be used in, or made by, the process. See MPEP § 802.01 and § 806.06. In the instant case, the 2'-O-substituted CpG containing phoshorothioate oligonucleotide of Group I is not disclosed or recited as being capable of use in the method of Group II. In fact, the amendments to claims 3-5 of Group II specifically exclude 2'-O-substituted CpGs as an alternative for use in the method.

Therefore, because these inventions are distinct for the reasons given above, and the searches required for each are divergent and not coextensive, and because a search and examination of each of the Inventions in a single application would present a serious burden on the Examiner, restriction for examination purposes as indicated is proper.

Inventions II and III are directed to related method. The related inventions are distinct if the (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the inventions as claimed have materially different designs. The method of Group III requires the administration of 2'-O-substituted CpG containing oligonucleotides, which are not specifically required by, and in fact have been expressly excluded from the method of Group II. Thus, the different methods requires the use of structurally and functionally distinct molecules, having different chemical compositions and different relative physical and biological properties.

For the same reasons, the inventions as claimed do not encompass overlapping subject matter (MPEP 806.05). Furthermore, there is nothing of record to show them to be obvious variants of one another.

Furthermore, searching and examining each of these inventions in a single application presents a serious burden on the examiner, since each method would require different keyword searches and considerations of the patent and non-patent literature with regard to novelty, obviousness, written description, and enablement. In particular, with the elimination of a common CpG modification, the examiner is now required to search and consider multiple types of CpG modifications, not shared by each of the groups.

Therefore, because these inventions are distinct for the reasons given above, and the searches required for each are divergent and not coextensive, and because a search and examination of each of the Inventions in a single application would present a serious burden on the Examiner, restriction for examination purposes as indicated is proper.

***Further restriction to a single type of modified CpG containing oligonucleotide (Group II, claims 3-5)***

Should applicant elect to prosecute Group II, applicant must further elect a single type of CpG modification. This is not a species election, but an election of a single independent or distinct invention.

Each of claims 3-5 is considered to be drawn to a plurality of related but distinct methods. The related methods are distinct if the (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the

inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the methods differ with regard to the physical and chemical characteristics of the CpG containing oligonucleotide. In particular, the molecules differ with regard to the type of chemical modification applied to the CpG unit. The oligonucleotides thereof differ one from the other, both structurally and functionally inasmuch as each molecule comprises a different type of modified CpG dinucleotide. Therefore, each claim recites a plurality of distinct molecules for use in the instant method. Since the alternatives are not claimed for use together, and since the alternatives have materially different designs, and since there is no disclosure of record to indicate the alternatives are obvious variants of one another, the methods of using said products do not overlap in scope and are distinct one from the other.

The Examiner acknowledges the practice for restriction among alternatives of a Markush group pursuant to MPEP 803.02, which states in part that if the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction.

Since the decisions in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. *In re Harnish*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where

compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

In the instant case, while the alternative molecules may share a common utility, the molecules do not share a substantial structural feature disclosed as being essential to that utility—the molecules are structurally distinct, one from the other. Moreover, the patentability of the instant molecules would appear be directly related to the particular type of CpG modification present in the phosphorothioate molecule. In this way, an alkylphosphonate CpG containing oligonucleotide is patentably distinct from, and does not share a significant structural feature with an oligonucleotide comprising an inverted CpG or 2'-5' CpG containing oligonucleotide. Furthermore, for purposes of a complete search and examination, a sufficiently few number of distinct alternatives is considered to be one (1).

See also *Official Gazette*, 1316 O.G. 122 (March 27, 2007), stating that "Polynucleotide molecules will be considered for independence, relatedness, distinction and burden as for any other type of molecule."

Searching and examining each of these molecules, and thereby, methods, in a single application would present a serious burden on the examiner, since each group would require different keyword searches (i.e., different fields of search) and different considerations of the patent and non-patent literature with regard to novelty, obviousness, written description, and enablement.

Therefore, because these inventions are distinct for the reasons given above, and the searches required for each are divergent and not coextensive, and because a search and

examination of all of the Inventions in a single application would present a serious burden on the Examiner, restriction for examination purposes as indicated is proper.

***Rejoinder***

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double

patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

***Prior art made of record but not currently relied on***

The following prior art is made of record and is not relied upon, but is considered pertinent to applicant's disclosure.

Hoke et al. (US Patent 5,506,212) "Oligonucleotides with substantially chirally pure phosphorothioate linkages" taught CpG containing, phosphorothioate antisense oligonucleotides comprising stereospecific internucleoside linkages. See especially Table 1, column 14.

***Conclusion***

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louis V. Wollenberger whose telephone number is 571-272-8144. The examiner can normally be reached on M-F, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571)272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Louis Wollenberger/
Examiner, AU 1635
October 30, 2007